THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

OFFICE OF HUMAN RESEARCH ETHICS
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To: Tina Stevens
Epa
CB:7315, MD58A USEPA , 104 Mason Farm Rd , Chapel Hill , NC , 27599

From: Biomedical IRB

Date: 5/12/2011

RE: IRB review of Unanticipated Problem report

Submission Type: Unanticipated Problem
Study #: 09-1344

Study Title: Cardiopulmonary Responses to Exposure to Ozone and Diesel Exhaust With Moderate Exercise in Healthy Adults

Submission Description:

A study participant experienced a persistent cough possibly related to their participation in a research protocol at the Human Studies Facility of the EPA

Based on the IRB's review of your report of an unanticipated problem, it has been determined that no additional information is required and no changes in the study are warranted.

CC:
Michael Madden, Environmental Protection Agency
Michael Schmitt
David Diaz-Sanchez
Howard Kehrl, Medicine
Howard Kehrl, (EPA), Non-IRB Review Contact

IRB Number:	09-1344	**Study Status:**	Approved
PI:	Tina Stevens	**IRB:**	Biomedical
Sponsor:	US Environmental Protection Agency - Contracts		
Study Title:	Cardiopulmonary Responses to Exposure to Ozone and Diesel Exhaust With Moderate Exercise in Healthy Adults		

Certified:	05/12/2011
Reference ID:	2577

>> Brief Description of Event

A study participant experienced a persistent cough possibly related to their participation in a research protocol at the Human Studies Facility of the EPA

A1) Did this event occur at a site for which a UNC-Chapel Hill IRB has direct oversight responsibility or involve a research participant at one of those sites? Yes

A2) Was the event unexpected in nature, severity, or frequency? Yes

Please explain:

The occurrence of a cough after exposure to ozone is not unexpected. This is a typical short term response to this pollutant. Acute exposure to diesel exhaust or ozone has not been shown to induce a persistent cough. However, on 4/27 the volunteer presented to the EPA Medical Station stating that he had a persistent cough since his last exposure on 2/18. He was seen by Dr. Kehrl who thought his cough likely was due to a condition similar to cough variant asthma or post viral persistent cough and treated him with prednisone.

A3) Do you think the event was related or possibly related to this research? Yes

Please explain:

This event may possibly be related to the exposure. However, exposure to diesel exhaust or ozone has not been shown to cause a persistent cough.

A4) Does the event suggest that the research places subjects or others at a greater risk or harm than was previously known or recognized?

Economic: No
Legal: No
Physical: Don't Know
Psychological: No
Social: No

Please explain all "yes" or "don't know" responses

Although this subject had developed a cough, the previous 6 subjects exposed to diesel exhaust and ozone combined did not.

>> Information About the Event

B1) Date of Event: 04/27/11

B2) Location of Event: US EPA Human Studies Facility

B3) Full Description of Event.

The study participant was a 23 year old male with a previous history of volunteering for EPA studies without incident. On 2/17 the subject was exposed to diesel exhaust and ozone combined. During the first 15 min of exposure on 2/17, the subject coughed several times while in the chamber. When questioned about his response, he said he felt fine and wanted to continue the study. He was monitored for lung function decrements, oxygen saturation, minute ventilation, and cardiac funciton during the exposure and 4 hrs post exposure. The pulmonary function and cardiac endpoints were within an acceptable range at discharge. On 2/18, he was exposed to ozone alone, with no unexpected changes in these endpoints. On 3/9, he returned for his second arm of the study. He came presenting a cough and was not exposed. He reported to the Human Study Facility on 4/27 complaining of an ongoing cough and was seen by a physician.

>> Was this a serious adverse event?

C1) Did the event result in death? No

C2) Was the event life-threatening (i.e., placed the subject at immediate risk of death from the event, as it occurred)? No

C3) Did the event result in inpatient hospitalization or prolongation of existing hospitalization? No

C4) Did the event result in a persistent or significant disability/incapacity? Yes

Please explain:

At present, the subject reports cough interferes with social interacitons and impairs his ability to exercise. However, he reports the cough is starting to improve and it may completely resolve with time.

C5) Did the event result in a congenital anomaly/birth defect? No

C6) Based upon appropriate medical judgment, did the event jeopardize the subject's health and/or require medial or surgical intervention to prevent one of the other outcomes listed above, e.g., allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse?
Yes

The subject was treated with 60 mg of prednisone for one week which did not imporve the cough. He also had a PA and lateral chest x-ray which was normal. His spirometry volumes and flow rates were the same as during his training session.

>> Protocol/Consent Forms

D1) Given this event's occurrence, are there revisions to the study or consent documents that you would like to submit at this time? No

>> Corrective Action

E1) Have you established a corrective action plan to prevent future occurrence of the event? Yes

Describe the corrective action plan:

Subjects that present a cough within the first 15 minutes of exposure will be removed from the chamber.

>> Attachments

There are no attachments for this event